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OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

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MEMORANDUM

SUBJECT: **Ethofumesate**: Registration Review: Preliminary Problem Formulation for Environmental Fate, Ecological Risk, Endangered Species, and Drinking Water Exposure Assessments

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1. Executive Summary

The Environmental Fate and Effects Division (EFED) has completed the problem formulation for the ecological risk, environmental fate, endangered species, and drinking water assessments to be conducted as part of the Registration Review of ethofumesate (PC Code 110601). The problem formulation describes the methods planned to be used during the completion of the drinking water and ecological risk assessments in support of registration review and provides an overview of the environmental fate, ecological effects, and potential risks associated with the use of ethofumesate as well as uncertainties unique to the risk assessment of ethofumesate. This document also identifies additional studies that would be beneficial to conducting an ecological risk assessment. Major findings include:

EFED recommends the following environmental fate and ecotoxicity studies to reduce uncertainty in the risk assessment:

- 835.4100: Aerobic Soil Metabolism (**TGAI or PAIRA**)
- 835.4200: Anaerobic Soil Metabolism (**TGAI or PAIRA**)
- 835.4300: Aerobic Aquatic Metabolism (**TGAI or PAIRA**)
- 835.4100: Anaerobic Aquatic Metabolism (**TGAI or PAIRA**)
- 850.1010: Aquatic Invertebrate Acute Toxicity Test, Freshwater Daphnids (TGAI)
- 850.1350: Estuarine/marine invertebrate chronic toxicity; Mysid shrimp (*Mysidopsis bahia*) (**TGAI**)
- 850.2100: Avian acute toxicity; Passerine species (**TGAI**)
- 850.2200: Avian dietary toxicity; bobwhite quail (*Colinus virginianus*) or mallard duck (*Anas platyrhynchos*) (**degradate NC 8493**)
- 850.4500: Algal toxicity; Freshwater diatom and marine diatom (*Skeletonema costatum)* (**TGAI**)[1]
- 850.4550: Cyanobacteria toxicity (**TGAI**)[1]
- Non-guideline Tier I: Honeybee adult chronic oral exposure (**TGAI**)
- Non-guideline / OECD TG237 Tier I: Honeybee larval acute oral exposure (**TGAI**)
- Non-guideline Tier I: Honeybee larval chronic oral exposure (**TGAI**)
- Non-guideline Tier II: Residue in pollen and nectar (recommendation conditional if risks identified in Tier I studies) (**TEP**)
- Non-guideline Tier II: semi-field testing for pollinators (tunnel and feeding studies) (recommendation conditional if risks identified in Tier I studies) (**TEP**)
- 850.3040: Tier III full-field testing for pollinators (recommendation conditional if risks identified in Tier II studies) (**TEP**)

The following label uncertainties were also identified (details in Section 3):

- Many of the labels did not provide information on the maximum number of applications allowed per year, the maximum annual rate (in terms of lbs ai/A), or the minimum re-application interval. While this information can generally be calculated on a per crop

[1] Normally testing with a TEP substance is preferred. TGAI testing is recommended for consistency with existing aquatic plant toxicity tests.

cycle basis, EFED recommends the labels be clarified, to include application information on a pound/acre annual basis. **Appendix 1** has more information on the application rates to be used in the assessment and any assumptions which may be made.

2. Introduction

Ethofumesate is a pre and post-emergence herbicide in the benzofuranyl alkylsulfonate class, and was first registered in 1977. It is currently formulated as a flowable, emulsifiable, and soluble concentrate and is used to control annual grasses and annual broadleaf weeds. Ethofumesate is absorbed by emerging shoots and roots (foliar absorption is reduced as leaves/cuticles develop) and acts as a seedling shoot inhibitor which affects developing leaves in the growing points of susceptible seedling plants. Ethofumesate is translocated to foliage following emerging shoot and root absorption, however it is not translocated from treated foliage.

Ethofumesate applications are made pre-plant, pre-emergence, and post-emergence with aerial or ground equipment. Ethofumesate is soil incorporated when applied to soil pre-plant. It can also can be soil applied without incorporation but requires rainfall or irrigation within three weeks. Application without incorporation can also be made pre or post-emergence, again with rainfall or irrigation required. The maximum annual rate identified and modeled for the 2004 RED was 9.0 lbs ai/acre, applied over multiple applications; the current maximum application rate is lower. The current maximum single application rate for agricultural uses is for sugar beets at 3.75 lb ai/A (annual rate not stated but is stated per crop cycle) as a flowable or emulsifiable concentrate, while the maximum non-agriculture single application use rate is for ornamental sod farms (turf) with a single application of 1.875 lb ai/A. **Appendix 1** includes application information for most of the currently registered uses of ethofumesate.

The major use of ethofumesate is on sugar beets (**Table 2.1**), with other food uses including bulb onions, carrots, garden beets, garlic, and shallots. Registered non-food uses are for seed crops, grasses grown for seed, turf, and sod farms. According to the Biological and Economics Analysis Division (BEAD), sugar beets accounted for an average of 300,000 lbs per year with the average percent crop treated at 30% with a maximum percent crop treated at 75% (USEPA 2015). **Table 2.1** shows usage information for the largest agricultural uses (data from 2004 through 2013).

Table 2.1. Average Annual Ethofumesate Agricultural Uses (data from 2004 through 2013).

		Annual Average	Percent Crop Treated	
	Crop	**Lbs. AI**	**Average**	**Maximum**
1	**Garlic***	**<500**	**<1**	**<2.5**
2	**Onions**	**10,000**	**20**	**40**
3	**Sugar Beets**	**300,000**	**30**	**75**

* Based on CA DPR data only (80% or more of U.S. acres grown are in California).

Ethofumesate is not currently co-formulated with other registered pesticides. There is an EUP, 264-EUP-138, from 2003 which was co-formulated with desmedipham and phenmedipham.

EFED evaluated the most recent ecological risk assessments for ethofumesate in association with updated toxicity, exposure, and usage information to determine if sufficient data are available and

if further updates are needed to support registration review. The most recent ecological risk assessments are the 2004 assessment for the Re-registration Eligibility Document (RED) and the 2005 amendment to that document (DP: D296942). In addition, EFED considered the latest Agency science policies and risk assessment methodologies. The structure of ethofumesate and its degradates, as well as the chemical names and other identifiers, can be found in the chemical identity table attached to this document **(Appendix 3).**

3. Use Characterization

Ethofumesate is an herbicide with pre-plant, pre-emergence, and post-emergence applications made by both aerial and ground application methods. It is registered for use on, vegetables (e.g., sugar beets, carrots, onions), turf, sod farms, and seed crops (see **Appendix 1** for a full list). There are three active technical registrations for ethofumesate, which is formulated into 13 active registered Section 3 end-use products as emulsifiable concentrates, flowable concentrates, and soluble concentrates. Applications are made by aerial or ground spray using aircraft, boom sprayer, ground sprayer, banded treatments, broadcast, and soil incorporations. The chemical profile produced by BEAD, located on regulations.gov in the registration review docket for ethofumesate, lists the use patterns for the current uses of ethofumesate. EFED will use application scenarios that result in maximum exposure for a given use for the risk assessment. Failure of the labels to specify the appropriate application interval, or the annual maximum rate (lb ai/A/year), may result in conservative assumptions.

For ethofumesate, several label issues were identified. **Appendix 1** includes a summary of missing information and the assumptions which may be made in the absence of this information. Specifically:

- There is no annual maximum application rate stated or the maximum application use rate is stated in terms of crop growing season rather than the annual rate for the following Registration #s: 264-612, 264-613, 264-615, 70506-106, 70506-107, 70506-283, 87290-1, 87290-2).
- Additionally, the labels are not clear on number of applications allowed per year for the following Registration #s: 264-612, 264-613, 264-615, 70506-106, 87290-1. In the absence of yearly information, multiple seasons or crop cycles may be assumed for some crops when performing the risk assessment, based on input from the Biological and Economics Analysis Division (BEAD). Any labels with multiple applications should also provide minimum re-treatment intervals.
- Some single application rates are listed on the label in terms of volume of product instead of lb/ai for the following Registration #s: 264-612, 264-613, 264-615, 70506-106, 70506-107, 70506-283, 87290-1, 87290-2). The maximum single application rates can be calculated when certain other information is provided; however, EFED recommends stating all single, seasonal, and/or annual application rates in terms of lbs ai/A.

4. Conclusions from Previous Risk Assessments

a. Ecological Risk Assessment

The Agency completed a Re-registration Eligibility Document (RED) for ethofumesate which includes the most recent complete ecological risk assessment and the basis for this problem

formulation. The EFED chapter for the RED was completed on June 16, 2004 and revised on August 31, 2005 (USEPA, 2004a and USEPA 2005; D296942) for all registered uses. The RED concluded the primary risk for freshwater fish (acute) and terrestrial plants. Based on predicted EECs and available toxicity data, there were no exceedances of any LOC for freshwater invertebrates (acute/chronic), estuarine/marine fish (acute) and invertebrates (acute), non-target aquatic plants, birds (acute/chronic), or mammals (acute chronic). There were no data available to assess chronic risk to estuarine/marine organisms. At the time of the RED terrestrial invertebrate risks were not quantitatively assessed, but ethofumesate was noted to be classified as practically non-toxic to honey bees (LD_{50} of >50 µg ai/bee) on an acute oral/contact basis. Several ethofumesate degradates were identified in the RED; however they were not modeled for the ecological risk assessment or drinking water assessment. Sections 5 and 8a have more information on these degradates and how they may be considered in the Registration Review risk assessment. **Table 4.1** below summarizes risk concerns and issues from the ethofumesate RED.

Table 4.1. Summary of Risk Concerns and Issues Identified for Ethofumesate in Previous Assessments

Birds	Mammals	Terr. Plants	Terr. Inverts	Fish	Aquatic Inverts	Aquatic Plants	Degradates of Concern
No	No	Yes[1]	NA	Yes[2]	No	No	No[3]

"Yes" = Risk concerns or issues were identified or presumed from lack of data in previous assessments; **"No"** risk concerns or issues were not identified in previous assessments
N/A = Not assessed
[1] = Listed and non-listed monocot and dicots
[2] = Listed only – Freshwater fish only assessed
[3] = The RED identified several degradates of potential concern; however, they were not considered as part of the assessment

b. Drinking Water Exposure Assessments

The most recent drinking water assessment for ethofumesate was conducted to support the Reregistration Eligibility Decision (RED) process for various agricultural crops and non-agricultural uses (USEPA 2004b; D296949). The recommended estimated drinking water concentrations (EDWC) in surface water and groundwater are listed in **Table 4.2**.

Table 4.2. The Upper Bound EDWCs for Ethofumesate

Drinking Water Sources	Acute (µg/L)	Non-cancer Chronic (µg/L)	Cancer Chronic (µg/L)
Surface water	203.1[1]	39.6[2]	26.0[3]
Groundwater	8.4	8.4	8.4

[1] FL Vegetable Scenario
[2] FL turf Scenario
[3] MN Sugarbeet Scenario

c. Clean Water Act Programs

Ethofumesate is not identified as a cause of impairment for any water bodies listed as impaired under section 303(d) of the Clean Water Act[2]. No Total Maximum Daily Load (TMDL) criteria have been developed for ethofumesate. Aquatic benchmarks have been established for

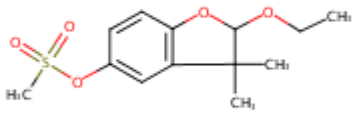
[2] http://iaspub.epa.gov/waters10/attains_nation_cy.control?p_report_type=T#tmdl_by_pollutant

ethofumesate and are available at: http://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/aquatic-life-benchmarks-pesticide-registrationAny data submitted or otherwise located as part of the registration review process may be used to update aquatic life benchmarks if applicable.

5. Environmental Fate and Transport

Ethofumesate is a chiral compound containing a racemic mixture of two enantiomers (R, S). The available environmental fate and ecological effects data on ethofumesate represent only the racemic mixture. Ethofumesate is a water soluble (53.7 mg/L @ 30°C) chemical. Low vapor pressure (2.8 x 10^{-07} mm Hg) and Henry's Law constant (1.53 x 10^{-09} atm·m3/mol) of ethofumesate suggest that volatilization is not a major route of dissipation from soil and water. The octanol water partition coefficient (log Kow of 2.8) suggests that it is not a bioaccumulative chemical. Selected physical and chemical and environmental fate properties are presented in **Table 5.1**.

Table 5.1. Physical and Chemical and Environmental Fate Properties of Ethofumesate

Property	Value	Source
Common Name	Ethofumesate	MRID 453954-01-05
CAS Registry No.	26225-79-6	MRID 453954-01-05
PC Code	110601	http://iaspub.epa.gov/apex/pesticides/f?p=chemicalsearch:1
Structure		TOXNET
Chemical Name (CAS)	2-ethoxy-2,3-dihydro-3,3-dimethyl-5-benzofuranyl methanesulfonate	MRID 469501-04
IUPAC Name	(*RS*)-2-ethoxy-2,3-dihydro-3,3-dimethylbenzofuran-5-yl methanesulfonate	http://www.alanwood.net/pesticides/ethofumesate.html
SMILES notation	CCOC1C(C2=C(O1)C=CC(=C2)OS(=O)(=O)C)(C)C	EPI Suite, v4.1
Molecular Formula	$C_{13}H_{18}O_5S$	MRID 453954-01-05
Physical and Chemical Properties		

Property	Value	Source
Molecular Weight	286.3	
Physical State	Solid (powder) @ 20°C	MRID 453954-05
Vapor pressure	2.9 x 10^{-05} PA (2.18 x 10^{-07} mm Hg) @ 25 °C	MRID 453954-04
Henry's Law constant	1.53 x 10^{-09} atm x m^3/mol	Estimated
Specific Gravity/ Density	1.28 g/ml @ 20°C	MRID 453954-05
Solubility in water	53.7 mg/L @ 30°C	MRID 453954-05
Solubility in organic solvents n-Hexane Tolune Dichloromethane Methanol Acetone Ethyl Acetate	 <10 g/L @ 30°C 666-800 @ 30°C >1000 @ 30°C 100-114 @ 30°C >1000@ 30°C 800-1000 @ 30°C	MRID 453954-05
log K_{ow}	2.8	MRID 453954-05
Environmental Fate Properties		
Hydrolysis half-life pH = 5 pH = 7 pH = 9	 Stable Stable Stable	MRID 115080
Photolysis half-life in water	14 days Major Degradate Unidentified (Unknown A) 17.6% @ day 6	MRID 46157901
Photolysis half-life in soil	13.8 days Major Degradate 8493(2,3-dihydro-2-hydroxy-3, 3-dimethyl-5-benzofuranyl methanesulphonate): 29.8% @ day 9	MRID 41214205
Aerobic soil metabolism half-life	83 days in silt loam 122 days in Sandy loam soil Major Degradate CO_2: 25% @ day 365 Nonextractable Residue: 57% @ day 365	MRID 42413001
Anaerobic soil metabolism half-life	759 days in Sandy loam soil No Major Degradate Nonextractable Residue: 57% @ day 365	MRID 42413002

Property	Value	Source
Aerobic aquatic metabolism half-life	105 days in River water-loamy sand sediment from Germany 156 days in Pond water-clay loam sediment from Germany Major Degradate Unidentified compound: 18% @ day 103 in total system. Nonextractable Residue: 52.2 @ day 30.	MRID 46096201
Terrestrial field dissipation half-life	75 to 120 day days in California 95 to 150 days in North Dakota	MRID 41997205
Soil adsorption coefficient K_F and K_{Foc} (L/kg)	**K_F** 0.73 for sand 2.35 for sandy loam 5.32 for silty clay loam 6.16 for clay **K_{Foc}** 209 for sand (0.35% organic carbon) 124 for sandy loam (2.35% organic carbon) 166 for silty clay loam (5.32% organic carbon 126 for clay (6.16 % organic carbon) 1/N values: 0.82-0.93	MRID 41214212
Column leaching (% parent in leachate; % identified residues in leachate)	Maximum 3.11% of ^{14}C was detected in leachate. Detection of ethofumesate and NC 20465 were negligible (<0.3%). Ethofumesate may have degraded to CO_2 during aging period. Un-extractable residue accounted for 32.4% of applied	MRID 42438001
Laboratory accumulation in fish bioaccumulation factor (*Lepomis macrochirus*) Depuration	17x in edible tissues 595x nonedible tissues 67x for whole body Approximately 99% of the accumulated residue depurated by day 3.	MRID 41970704

The major route of dissipation of ethofumesate appears to be via abiotic processes (aqueous and soil photolysis; DT_{50s} of ≈14 days), however, the chemical is stable to hydrolysis at pH 5, 7, and 9 in aqueous buffered solutions. The principal degradates (≥10%) detected in abiotic studies were NC 8493 and two unidentified compounds. In both aerobic and anaerobic soil systems, ethofumesate dissipation appears to be dependent on microbial mediated mineralization to CO, and with residues incorporated as non-labile soil bound residues. Three degradates, NC 8493, NC 9607, and NC 20645, were detected in both the aerobic and anaerobic metabolism studies but at less than 10% of applied. Ethofumesate degraded slowly in aerobic aquatic system with DT_{50} for the total system ranging from 105 to 156 days. Several unidentified degradates were detected

including one which was present at greater than 10% of applied (Table 5.1). The non-extractable fraction (14.2 to 52.3%) was a major sink for the applied ethofumesate, while mineralization accounted for 1.5 to 23.4% AR in laboratory aerobic soil and aerobic aquatic metabolism studies.

The DT_{50}s of 75 to 150 days in terrestrial field studies indicate that ethofumesate may dissipate slowly depending on the climatic/regional conditions. The dissipation rates of 75 to 100 days in California were slightly faster than the 95 to 150 days in cooler region, North Dakota. The analytical method employed in the terrestrial field dissipation studies does not distinguish between parent and degradate and therefore, no information is available on the presence of degradates under actual field use. Ethofumesate was not detected below the 6 inch depth except for one sample at the California site and was not detected below the 12 inch depth at the North Dakota site.

The batch equilibrium study suggests that ethofumesate is moderately mobile (K_{Foc} of 124 to 209 L/Kg) according to the FAO classification of mobility in soil (FAO, 2000). However, ethofumesate was not detected below the 6 inch depth except for one sample at the California site and was not detected below the 12 inch depth at the North Dakota site in terrestrial field studies. Ethofumesate has the potential to move off the site of application during rainfall/irrigation by erosion/runoff on soil particles and by drift during application in the field.

Transformation Products

The principal degradates detected in abiotic studies were Compound A and an unidentified compound detected in aqueous photolysis, and NC 8493 in soil photolysis studies, while NC 10458 was detected at less than 10% in the aqueous photolysis study. In both aerobic and anaerobic soil systems, ethofumesate dissipation appears to be dependent on microbial mediated mineralization to CO_2 and with residues incorporated as non-labile soil bound residues. Three degradates, NC 8493, NC 9607, and NC 20645, were detected in both the aerobic and anaerobic metabolism studies but at less than 10% of applied. In aquatic systems, several unidentified degradates were detected including one which was present at greater than 10% of applied. The analytical method employed in the terrestrial field dissipation studies does not distinguish between parent and degradate and therefore, no information is available on the presence of degradates under actual field use conditions. The maximum percent formation of major and minor degradates in various media are listed in **Appendix 3**.

6. Receptors

a. Effects to Aquatic Organisms

Table 6.1 provides a summary of the aquatic taxonomic groups, and the available endpoints for the most sensitive surrogate species tested to characterize the potential acute and chronic ecological effects of ethofumesate. A full list of available studies is provided in **Appendix 4**. In general, ethofumesate is slightly toxic to fish species, practically non-toxic to freshwater invertebrates, and moderately toxic to estuarine marine invertebrates on an acute exposure basis. No chronic data are available for estuarine/marine fish or invertebrates. Chronic exposure data for freshwater taxa show effects on growth and weight of freshwater fish and offspring production of freshwater invertebrates.

Table 6.1. Summary of the Endpoints from Aquatic Toxicity Studies to Characterize Risk for Ethofumesate

Taxonomic Group	Study Type	Surrogate Species	Toxicity Value	Acute Toxicity Classification	Source and Classification
Freshwater Fish	Acute	Rainbow trout (*Oncorhynchus mykiss*)	LC_{50} = 11.52 mg ai/L NOAEC (visually estimated) = 3.73 mg ai/L LOAEC = 7.31 mg ai/L LOAEC based on sublethal effects: darkened appearance, loss of equilibrium, lethargy and loss of balance	Slightly toxic	46578951 Acceptable
	Chronic (Early Life-Stage)	Fathead minnow (*Pimephales promelas*)	NOAEC = 2.56 mg ai/L LOAEC = 4.17 mg ai/L Based on length and wet weight	--	42008901 Acceptable
Estuarine/marine fish	Acute	Sheepshead minnow (*Cyprinodon variegatus*)	LC_{50} = 25.0 mg ai/L NOAEC = 12.0 mg ai/L LOAEC = 19.0 mg ai/L LOAEC based on sublethal effects: lethargy and loss of equilibrium	Slightly Toxic	42409301 Acceptable
Freshwater invertebrates	Acute	Waterflea (*Daphnia magna*)	EC_{50} = 294 mg ai/L Sublethal effects not reported	Practically non-toxic	115063 Supplemental
	Chronic	Waterflea (*Daphnia magna*)	NOAEC = 0.3 mg ai/L LOAEC = 0.6 mg ai/L Based on offspring production)	--	42871901 Acceptable
Estuarine/marine	Acute	Eastern oyster	EC_{50} = 2.6 mg	Moderately toxic	42388101

Taxonomic Group	Study Type	Surrogate Species	Toxicity Value	Acute Toxicity Classification	Source and Classification
invertebrates		(*Crassostrea virginica*)	ai/L NOAEC (estimated) = 0.8 mg ai/L LOAEC (estimated) = 2.0 mg ai/L Based on shell deposition		Acceptable
	Acute	Mysid shrimp (*Americamysis bahia*)	LC_{50} = 5.3 mg ai/L NOAEC < 2.5 mg ai/L LOAEC = 2.5 mg ai/: LOAEC estimated based sublethal effects: Surfacing, lethargy, erratic swimming	Moderately toxic	42364502 Acceptable
Aquatic plants	Non-vascular (TGAI[1])	Green algae (*Raphidocelis subcapitata*)	<u>Cell Density, Growth Rate, and Biomass</u> EC_{50} > 2.76 mg ai/L NOAEC > 2.76 mg ai/L LOAEC > 2.76 mg ai/L No effects	--	41687601 Acceptable
	Vascular (TGAI[1])	Duckweed (*Lemna minor*)	<u>Number of fronds</u> EC_{50} = 39.0 mg ai/L NOAEC = 0.76 mg ai/L LOAEC = 1.9 mg ai/L <u>Growth</u> EC_{50} > 52.8 mg ai/L NOAEC = 4.3 mg ai/L LOAEC = 10.0 mg ai/L <u>Biomass</u>	--	46450701 Supplemental

Taxonomic Group	Study Type	Surrogate Species	Toxicity Value	Acute Toxicity Classification	Source and Classification
			EC_{50} > 52.8 mg ai/L NOAEC = 0.76 mg ai/L LOAEC = 1.9 mg ai/L		

[1] TGAI = Technical Grade Active Ingredient.

b. Effects to Terrestrial Organisms

Table 6.2 provides a summary of the terrestrial taxonomic groups and the available endpoints for the most sensitive surrogate species tested to characterize the potential acute and chronic ecological effects of ethofumesate. Ethofumesate is practically non-toxic to both birds and mammals on an acute exposure basis and no effects were seen for either group in chronic toxicity tests. Honeybee data suggest ethofumesate is practically non-toxic to adult honeybees on both an acute oral and acute contact basis; however, toxicity based on a chronic exposure and toxicity to other life stages (larvae) is uncertain. There are no toxicity data available for the degradates although ECOSAR modeling suggests the major degradates (NC 8493, Component A) are at least of comparable toxicity to the parent ethofumesate. A third major degradate exists but the structure is unidentified and ECOSAR toxicity estimates cannot be obtained for this degradate (Unidentified). See Appendix 3 for information on major and minor degradate fate information.

Table 6.2. Summary of the Most Sensitive Endpoints from Terrestrial Toxicity Studies for Ethofumesate

Taxonomic Group	Study Type	Surrogate Species	Toxicity Value	Acute Toxicity Classification	Source and Classification
Birds	Acute oral	Bobwhite quail (*Colinus virginianus*)	LD_{50} > 8743 mg ai/kg-bw No effects	Practically non-toxic	115064 Acceptable
	Acute oral	Mallard duck (*Anas platyrhynchos)*	LD_{50} > 3445 mg ai/kg-bw No effects	Practically non-toxic	115065 Supplemental
	Acute dietary	Bobwhite quail (*Colinus virginianus*)	LC_{50} > 5200 mg ai/kg-diet NOAEC ≥ 5200 mg ai/kg-diet No effects	Practically non-toxic	41949201 Acceptable

Taxonomic Group	Study Type	Surrogate Species	Toxicity Value	Acute Toxicity Classification	Source and Classification
	Acute dietary	Mallard duck (*Anas platyrhynchos)*	LC_{50} > 5200 mg ai/kg-diet NOAEC ≥ 5200 mg ai/kg-diet No effects	Practically non-toxic	41949202 Acceptable
	Chronic reproduction	Bobwhite quail (*Colinus virginianus*)	NOAEC ≥ 3240 mg ai/kg-diet LOAEC > 3240 mg ai/kg-diet No effects reported	--	45818111 Acceptable
	Chronic reproduction	Mallard duck (*Anas platyrhynchos)*	NOAEC ≥ 3069 mg ai/kg-diet LOAEC > 3069 mg ai/kg-diet No effects reported	--	45855503 Acceptable
Mammals	Acute oral	Laboratory rat (Rattus norvegicus)	LD_{50} > 6400 mg ai/kg-bw No effects	Practically non-toxic	41214215 Acceptable
	Chronic Reproduction	Laboratory rat (Rattus norvegicus)	NOAEC ≥ 5000 mg ai/kg-diet LOAEC > 5000 mg ai/kg-diet No effects	--	92063034 Acceptable
Terrestrial insects	Acute contact	Honeybee (*Apis mellifera*)	LD_{50} > 50 µg ai/bee NOAEC ≥ 50 µg ai/bee No effects	Practically non-toxic	45638220 Acceptable
	Acute oral	Honeybee (*Apis mellifera*)	LD_{50} > 50 µg ai/bee NOAEC ≥ 50 µg ai/bee No effects	Practically non-toxic	41970703 Acceptable

Taxonomic Group	Study Type	Surrogate Species	Toxicity Value	Acute Toxicity Classification	Source and Classification
Terrestrial plants	Vegetative vigor	Monocot Onion (*Allium cep*a), corn (*Zea mays*), oat (*Avena sativa*), wheat (*Triticum aestivum*) Dicot carrot (*Daucus carota*, cucumber (*Cucumis sativus*), soybean (*Glycine max*), lettuce (*Lactuca sativa*), tomato (*Lycopersicum esculentum*), radish (*Raphanus sativus*)	Monocot (wheat) EC_{25} = 0.24 lb ai/A NOAEC = 0.16 lb ai/A Based on dry weight Dicot (Soybean)* EC_{25} = 0.09 lb ai/A EC_{05} = 0.003 lb ai/A NOAEC < 0.16 lb ai/A Based on height Dicot (Radish)* EC_{25} = 0.21 lb ai/A EC_{05} = 0.000024 lb ai/A NOAEC < 0.16 lb ai/A Based on dry weight Phytotoxic effects in all species included chlorosis, necrosis, leaf dormancy, stem desiccation.	--	45874701 Acceptable
	Seedling emergence	Monocot Onion (*Allium cep*a), corn (*Zea mays*), oat (*Avena sativa*), wheat (*Triticum aestivum*) Dicot carrot (*Daucus carota*, cucumber (*Cucumis sativus*), soybean (*Glycine max*), lettuce (*Lactuca sativa*), tomato (*Lycopersicum esculentum*), radish (*Raphanus sativus*)	Monocot (wheat) EC_{25} = 0.15 lb ai/A NOAEC = 0.08 lb ai/A Based on dry weight Dicot (lettuce) EC_{25} = 0.18 lb ai/A NOAEC = 0.16 lb ai/A Based on dry weight Phytotoxic effects in all species included chlorosis, necrosis, leaf dormancy, stem desiccation.	--	45814702 Acceptable

*Both dicots will be used to characterize risks based on radish having the less sensitive EC25 but more sensitive EC05 than soybean (more sensitive EC25 but less sensitive EC05)

c. Degradates

Toxicity data are not available for ethofumesate's major degradates of concern. ECOSAR methods were used to predict aquatic toxicity for the degradates based on their structural similarity to chemicals for which aquatic toxicity data are known (ECOSAR predictive software

is available publically though the Epi Suite™ program[3]). ECOSAR estimates for NC 8493 and Component A are presented in **Table 6.3** below. An additional major unidentified degradate exists (**Appendix 3**) but no structure has been identified and consequently toxicity is not estimated. To judge the reliability of the ECOSAR predictions, the estimates for ethofumesate were compared to empirical ethofumesate toxicity endpoints (**Table 6.3**). As previously mentioned, no toxicity data are available for any degradates so only the ECOSAR estimates for the listed degradates are included. The results suggest that ECOSAR is generally making good estimates of toxicity based on comparing known data to the estimates. The freshwater invertebrate endpoint is over estimated; however, it is still within one order of magnitude (of parent value in the toxicity study). The same is potentially true for green algae as the non-definitive endpoint showed only about 7% inhibition at 2.76 mg ai/L suggesting the actual endpoint is significantly higher than the reported value. If the green algae endpoint is higher (at least approaching the ECOSAR estimate) the other ECOSAR estimates suggest toxicity of NC 8493 is comparable to the parent (freshwater inverts) or within an order of magnitude (freshwater fish, green algae, and estuarine/marine fish). For Component A, making the same assumption about the green algae toxicity endpoint, ECOSAR predicts toxicity difference of an order of magnitude. There is some additional uncertainty suggesting the toxicity estimate of Component A is comparable to the parent. Since the predicted values are less toxic than the NC 8493 and even lower than the parent (data and estimates) assuming equal toxicity could be an overestimate.

Table 6.3. ECOSAR estimates (ester class) for ethofumesate degradates NC 8493 and Compound A as compared to known toxicity endpoints

Toxicity Test	Ethofumesate (effects studies)	Ethofumesate (ECOSAR estimate)	NC 8493 (ECOSAR estimate)	Component A (ECOSAR estimate)
Concentration (mg ai/L)				
Freshwater Fish 96-hr LC_{50}	11.2	13.06	101.59	438.91
Freshwater Invertebrate 48-hr LC_{50}	294	24.91	230.14	1115.74
Green algae 96-hr EC_{50}	>2.76	9.34	111.22	639.53
Estuarine/Marine Fish 96-hr LC_{50}	25	19.81	162.34	749.14

d. Ecological Incidents

The ecological incident information system (EIIS) is an OPP database that houses ecological incidents that have been reported to the Agency. When available, EIIS includes date and location of an incident, type and magnitude of effects observed in various species, use(s) of pesticides known or suspected of contributing to the incident, and results of any chemical residue analysis or other analyses conducted during incident investigation. EIIS incidents are categorized according to the certainty that the incident resulted from pesticide exposure. The Avian Monitoring System

[3] http://www2.epa.gov/tsca-screening-tools/epi-suitetm-estimation-program-interface

(AIMS) is a database administered by the American Bird Conservancy that contains publicly available data on reported avian incidents involving pesticides. Many of the incidents listed in this database are also in the EIIS. Searches of the Ecological Incident Information System (EIIS v. 2.1.1), and the Avian Incident Monitoring System (AIMS) were performed on 11/4/15.

While the search of AIMS did not return any incidents, EIIS returned five terrestrial plant incidents and one terrestrial animal incident associated with ethofumesate. A summary of each incident is below (**Table 6.4**):

Table 6.4. Ecological Incidents Involving Ethofumesate

Incident	Organism	Date	Location	Chemical(s)	Certainty	Use	Magnitude
I017162-007	Beets	1/27/2006	Fresno, CA	Progress (Phenmedipham, Desmedipham, and Ethofumesate)	Probable	Registered Use	75 acres
Grower applied a **higher rate of Progress** (Phenmedipham, Desmedipham, and Ethofumesate) **than recommended for the stage the crop was in**. This resulted in a yellowing and stunting of 100% of the beet crops that the Progress was applied to. Although the pesticide was applied at a higher than recommended rate for the crop stage, the grower still did not exceed the max label rate.							
I013246-041	Sugar Beets	6/20/2002	Richland, MT	Progress (Phenmedipham, Desmedipham, and Ethofumesate)	Probable	Unknown	600 acres
Aventis reported a complaint from Sidney, MT, that PROGRESS Herbicide damaged all 600 acres of a sugar beet crop. This was reported to Bayer Crop Science during July, 2002. The damage symptom was "stunting" and the Probable Cause #1 was said to be "adjuvant." This is a PA* severity type of incident.							
I013246-042	Sugar Beets	6/20/2002	Richland, MT	Progress (Phenmedipham, Desmedipham, and Ethofumesate)	Probable	Unknown	500 acres
Aventis reported a complaint from Sidney, MT, that PROGRESS Herbicide damaged 500 acres of a 1000-acre crop of sugar beets. This was reported to Bayer Crop Science during July, 2002. The damage symptom was "stunting" and the Probable Cause #1 was said to be "adjuvant." This is a PA* severity type of incident.							
I022708-005	Grass Seed	12/12/2010	Sacramento, CA	Nortron SC (ethofumesate)	Possible	Registered Use	53 acres
On December 12, 2010 in Sacramento County CA 100% of 53 acres of grass seed crop exhibited stand reduction and seedlings stunted after the product Nortron SC (ai ethofumesate) was applied. Phytotoxic reaction to product is alleged following application to grass seed crop. The Registrant suggested the probable cause may be plant stress.							
I023949-011	Onion	12/1/2011	Uvalde, TX	Nortron SC (ethofumesate)	Possible	Registered Use	30 acres
The onion crop exhibited stunting symptoms during late January and early February of 2012. The field was seen again on the 1st week in March 2012 and the onion showed severe stunting and reduced plant stand. The incident is under investigation. Alleged phytotoxic reaction to product following application to onion crop.							
I014123-007	Wheat	5/14/2003	Malheur, OR	Nortron SC (ethofumesate)	Possible	Unknown	62 acres
Alleged that carryover of the herbicide NORTON SC (Ethofumesate) affected the Spring Wheat crop. Symptoms were minor stand reduction and stunting.							
I024270-001	Honeybees	5/1/2012	Seneca, NY	clothianidin, cyprodinil, ethofumesate, fenbuconazole, methoxyfenozide,	Unlikely	Unknown	48 colonies

				thiacloprid, phosmet, captan, and cyhalothrin			
On May 1, 2012 in Seneca County, New York a beekeeper observed bees dying in 48 colonies. The hives had been providing pollination services to a 50 acre orchard containing apricot, plum and apple trees. The field adjacent to the orchard had been planted with corn around May 7. The field was planted using an air seeder. The beekeeper noted that the adjacent fields had been subject to a chemical burn down. The beekeeper suspects Round-up (ai glyphosate) was used. The beekeeper removed his bees from the orchard when the orchard owner wanted to apply Assail (ai acetamiprid). A lab from Penn State report detected the following pesticides in either bee tissue and/or pollen: clothianidin, cyprodinil, ethofumesate, fenbuconazole, methoxyfenozide, thiacloprid, phosmet, captan, and cyhalothrin							

*PA was an abbreviation noted in the incident report but not defined.

The aggregate Incident Data System (IDS) was also searched on 11/5/15. Registrants reported 4 minor plant damage incidents with ethofumesate between 2005 and 2008. Unless additional information on these aggregated incidents becomes available, they will be assumed to be representative of registered uses of ethofumesate in the risk assessment.

7. Exposure Pathways of Concern

The environmental fate properties and use patterns of ethofumesate indicate that direct spray, spray drift, leaching to ground water, and runoff represent potential transport mechanisms to aquatic and terrestrial organisms. Drinking water and inhalation exposure pathways were screened using the SIP (Screening Imbibition Program) and STIR (Screening Tool for Inhalation Risk) screening methods. Both SIP (drinking water) and STIR (inhalation) screenings identified the drinking water and inhalation exposure pathways of low concern (no LOC exceedances are expected) for birds and mammals **(Appendix 5)**. SIP and STIR are described in detail at: http://www2.epa.gov/pesticide-science-and-assessing-pesticide-risks/models-pesticide-risk-assessment

8. Analysis Plan

a. Stressors of Concern

i. Ecological Risk Assessment

The stressor of ecological concern for aquatic organisms is the parent ethofumesate. For aquatic exposures, degradates formed in the aquatic environment (Component A and Unidentified) are assumed to be equally toxic as parent based on lack of data (for both) and ECOSAR predictions (Component A only). At the time of the RED, major degradate NC 8493, and minor degradates NC 9607, and NC 20645 were considered for the aquatic assessment. However, an estimate of the total residue half-lives for these three degradates resulted in only a slight change in the 90th percentile value of the half-life for modeling (to represent parent plus degradate exposure) from 163 days to 169 days. Consequently, because predicted EECs would not significantly change from modeling the parent alone, ethofumesate was the only stressor of concern considered for the aquatic assessment. Neither, Component A, nor the Unidentified degradate were considered any further in the aquatic risk assessment in the RED.

The major degradates (component A, and unidentified) that form in the abiotic aquatic environment would only potentially contribute significantly to aquatic exposures via spray drift, while NC 8493 (forms in soil) would be expected to contribute to exposure most significantly through run off. Spray drift exposure is assumed to be minimal based on the maximum formation of 17% (Component A) from 12% of the original application reaching the aquatic environment. Component A and unidentified (forms in water) or NC 8493 (forms in soil), would have to be much more toxic than the parent to alter risk conclusions based on the amount estimated to reach the aquatic environment from spray drift (component A) or runoff (NC 8493). ECOSAR predicts at least equal toxicity of component A and NC 8493 to the parent, while no estimates are available for the unidentified degradate. Therefore, parent ethofumesate only will be considered for the aquatic assessment.

The stressors of ecological concern for terrestrial organisms are the parent ethofumesate and possibly the degradate NC 8493. For terrestrial organisms, the degradate NC 8493 is formed up to almost 30% in a soil photolysis study, which foraging birds could be exposed to. The lack of NC 8493 toxicity information for terrestrial organisms is an uncertainty. Acute oral data (results in a Section 18 - Emergency Exemption 9/16/77: Appendix 2) for the guinea pig and rat produced LD_{50} values of 900 and 1200 mg/kg-bw respectively, which is more toxic than the non-definitive (greater than) parent LD_{50} values. The toxicity of NC 8493 is unknown to birds and consequently, this degradate may be considered a stressor of concern for terrestrial organisms along with the parent ethofumesate.

ii. Drinking Water

A new drinking water assessment may be conducted, if warranted, to support future human health dietary risk assessments of ethofumesate for all currently registered uses. The Metabolism Assessment Review Committee (MARC) of the Health Effects Division (USEPA 2004c) predicted that degradates NC 8493, NC 9607, and NC 20645 were of toxicological equivalence to ethofumesate and should be included in the dietary assessment. However, the MARC also determined that based on the environmental fate properties of this chemical and the relatively low amounts of degradates detected in the laboratory environmental fate studies that only parent ethofumesate needs to be assessed for drinking water.

If drinking water assessment is warranted, it will be performed based on EFED's current guidance using appropriate surface and groundwater models. Descriptions of all executable versions of current models for drinking water exposure can be obtained from URL link: http://www2.epa.gov/pesticide-science-and-assessing-pesticide-risks/models-pesticide-risk-assessment

b. Measures of Exposure

EFED will use the latest standard available models to evaluate potential exposures to aquatic and terrestrial organisms as described at http://www2.epa.gov/pesticide-science-and-assessing-pesticide-risks/models-pesticide-risk-assessment. The parent ethofumesate will be considered in both terrestrial and aquatic exposures. The un-extracted fraction may be considered as a residue of concern for aquatic exposures, while the degradate NC 8493may be considered in the terrestrial assessment pending toxicity results.

i. Available Monitoring Data

The Agency is aware of monitoring conducted by federal and state agencies such as U.S. Geological Survey (USGS) National Water Quality Assessment (NAWQA) Data Warehouse and California Environmental Data Exchange Network (CEDEN). This exposure data will be considered in the assessment to the extent that data on ethofumesate and/or its degradates are available.

c. Measures of Effect

Toxicity data presented in Section 6 of this problem formulation will be used to calculate risk quotients. Any additional information submitted by the registrant or found in the open literature prior to conducting the risk assessment will also be considered. The open literature studies are identified using EPA's ECOTOXicology database (ECOTOX), which employs a literature search engine for locating chemical toxicity data for aquatic life, terrestrial plants, and wildlife. The evaluation of both sources of data can also provide insight into the direct and indirect effects of pesticides on biotic communities from loss of species that are sensitive to the chemicals and from changes in structure and functional characteristics of the affected communities.

9. Endangered Species Assessments

Consistent with EPA's responsibility under the Endangered Species Act (ESA), the Agency will evaluate risks to federally listed threatened and endangered (listed) species from registered uses of pesticides in accordance with the Joint Interim Approaches developed to implement the recommendations of the April 2013 National Academy of Sciences (NAS) report, *Assessing Risks to Endangered and Threatened Species from Pesticides*. The NAS report outlines recommendations on specific scientific and technical issues related to the development of pesticide risk assessments that EPA and the Services must conduct in connection with their obligations under the ESA and FIFRA. EPA will address concerns specific to ethofumesate in connection with the development of its final registration review decision for ethofumesate.

In November 2013, EPA, the U.S. Fish and Wildlife Service, National Marine Fisheries (the Services), and USDA released a white paper containing a summary of their joint Interim Approaches for assessing risks to listed species from pesticides. These Interim Approaches were developed jointly by the agencies in response to the NAS recommendations, and reflect a common approach to risk assessment shared by the agencies as a way of addressing scientific differences between the EPA and the Services. Details of the joint Interim Approaches are contained in the November 1, 2013 white paper, *Interim Approaches for National-Level Pesticide Endangered Species Act Assessments Based on the Recommendations of the National Academy of Sciences April 2013 Report*[4].

[4] http://www2.epa.gov/endangered-species/interim-approaches-pesticide-endangered-species-act-assessments-based-nas-report

Given that the agencies are continuing to develop and work toward implementation of the Interim Approaches to assess the potential risks of pesticides to listed species and their designated critical habitat, this ecological problem formulation supporting the Preliminary Work Plan for ethofumesate does not describe the specific ESA analysis, including effects determinations for specific listed species or designated critical habitat, to be conducted during registration review. While the agencies continue to develop a common method for ESA analysis, the planned risk assessment for the registration review of ethofumesate will describe the level of ESA analysis completed for this particular registration review case. This assessment will allow EPA to focus its future evaluations on the types of species where the potential for effects exists, once the scientific methods being developed by the agencies have been fully vetted. Once the agencies have fully developed and implemented the scientific methods necessary to complete risk assessments for listed species and their designated critical habitats, these methods will be applied to subsequent analyses of ethofumesate as part of completing this registration review.

10. Endocrine Disruptor Screening Program

Ethofumesate was not included in the first group of 67 chemicals included in the first group of chemicals issued an order to conduct Tier 1 Endocrine Disruptor Screening Program (EDSP) testing. For additional information the EDSP program visit: http://www2.epa.gov/endocrine-disruption/endocrine-disruptor-screening-program-edsp-overview.

11. Preliminary Identification of Data Gaps

a. Environmental Fate

Table 11.1 identifies environmental fate studies by MRID that offer data for each guideline requirement, as well as study classifications and whether or not further data are needed to support the risk assessment. There are no environmental fate studies available for either major degradate of ethofumesate (*i.e.*, NC 8493 and Component A detected in photolysis studies and unidentified degradate in aerobic aquatic metabolism study). Degradate NC 8493forms up to 30% in the terrestrial environment while Component A is not a major transformation product in the terrestrial environment. In the absence of data, EFED will assume these degradates are stable and use QSAR modeling (EPISuite ver. 4.0) to estimate the physical and chemical properties needed for modeling inputs. Additional environmental fate and physicochemical properties of major degradates can reduce the uncertainties in the aquatic exposure assessment. The un-extracted fraction (14.2 to 52.3%) was a major sink for the applied ethofumesate in laboratory aerobic soil and aerobic aquatic metabolism studies. There is uncertainty as to whether to consider the un-extracted fraction as a part of a residue of concern. Therefore, multiple polar and nonpolar solvents with different chemical properties should be explored for each pending soil and sediment study listed below. Additional information regarding the un-extracted fraction can be obtained from current "Guidance for Addressing Un-extracted Residues in Laboratory Studies."[5]

[5]http://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/guidance-addressing-unextracted-pesticide-residues

Table 11.1. Submitted Environmental Fate Data for Ethofumesate Parent

OCSPP Guideline	Data Requirement	Source MRID	Classification	Are data needed to conduct risk assessment?	Justification and Assumptions EPA Will Make in the Absence of Data
835.2120	Hydrolysis	115080	Acceptable	No	---
835.2240	Aqueous Photolysis	46157901	Acceptable	No	---
835.2410	Soil Photolysis	41214205	Acceptable	No	---
835.4100	Aerobic Soil Metabolism	42413001	Acceptable	Yes Partially fulfilled	OCSPP guidance recommends that these tests be performed with four soils. Two aerobic soil metabolism studies have already been submitted and classified as acceptable for risk assessment. An additional two studies are required under 40 CFR Part 158 for terrestrial outdoor uses. Because OCSPP uses an upper 90th percentile estimate of soil metabolism half-lives based on available study data for modeling purposes, any additional data can reduce uncertainty related to the exposure assessment as well as the half-life value used in modeling.
835.4200	Anaerobic Soil Metabolism	42413002	Acceptable	Yes Partially fulfilled	OCSPP guidance recommends that these tests be performed with four soils. One anaerobic soil metabolism study has already been submitted and is classified as acceptable for risk assessment. Additional data are required under 40 CFR Part 158 for terrestrial outdoor uses. Additional data are considered to have a low potential to add value to exposure assessments for the ecological risk and drinking water in presence of anaerobic aquatic metabolism (835.4400).
835.4300	Aerobic Aquatic Metabolism	46096201	Supplemental	Yes Partially fulfilled	The experimental design of the submitted study was inadequate to assess aerobic aquatic degradation because an aerobic soil/ sediment was not treated and flooded at the same time. This precludes the study from being considered an aerobic aquatic metabolism experiment. In addition, all degradates detected at >l0% of the applied were not identified. Additional data is needed to upgrade this study to be considered in risk assessment.
835.4400	Anaerobic Aquatic Metabolism	--	--	Yes	Data are required under 40 CFR Part 158. OCSPP guidance recommends that these tests be performed with two sediments. The assumption of compound stability will be

OCSPP Guideline	Data Requirement	Source MRID	Classification	Are data needed to conduct risk assessment?	Justification and Assumptions EPA Will Make in the Absence of Data
					made in the absence of acceptable data.
835.1230 835.1240	Adsorption/ Desorption and Leaching	42214212	Acceptable	No	---
835.1410	Volatility – laboratory	No Data	---	No	Not triggered based on low vapor pressure (2.8×10^{-7} torr at 25°C)
835.6100 164-1	Terrestrial Field Dissipation	41997205	Supplemental	No	---
850.6100	ECM/ILV (soil and water)	No Data	---	No	All field dissipation studies were conducted prior to April 19, 1996; therefore, Environmental Chemistry Method (ECM) and Independent Laboratory Validation (ILV) data are not required.
850.1730 165-4	Fish bioconcentration	41970704	Acceptable	No	---

b. Ecological Effects

Table 11.2 and Table 11.3 identify ecological effects studies by MRID that offer data for each guideline requirement, as well as study classifications and whether or not further data are needed to support risk assessment. Rationale for the additional data requested is presented below the tables. **There are missing chronic data for estuarine/marine organisms, pollinator larval toxicity (acute and chronic), and pollinator adult toxicity (chronic)**. **No toxicity data are available for any degradates of ethofumesate.**

For estuarine/marine fish, chronic risk concerns were not identified in the RED, and the endpoints affected in the freshwater fish ELS study were growth and length. With no reproductive effects noted in other organisms, a chronic estuarine/marine fish study would not be expected add significant value to the risk assessment. Consequently, while a definitive endpoint for an acute toxicity test with the fathead minnow would allow EFED to calculate a chronic endpoint with an ACR, the study is not being requested at this time. Chronic estuarine/marine risks for fish will be characterized based on the freshwater fish endpoints which the acute data suggest are of comparable toxicity.

No chronic data exist for estuarine/marine invertebrates. A life-cycle study with the mysid would reduce uncertainty in the risk assessment. Mortality was observed in the lowest test concentration of mysid, and both the mysid shrimp and oyster are more sensitive than the freshwater daphnid on an acute exposure basis. The greater sensitivity of estuarine/marine invertebrates increases the likelihood of a risk concern compared to their freshwater counterparts. A study to obtain a chronic endpoint would reduce any uncertainty in the risk conclusions. In the

absence of data, a chronic endpoint can be estimated by comparing the freshwater definitive endpoints to the estuarine/marine endpoints (ACR).

Based on the mode of action and as an herbicide, plants are the main group expected to be affected by ethofumesate. Terrestrial plant toxicity endpoints used to evaluate risks to non-listed species (NOAECs) were non-definitive for some plants in Tier II tests; however, IC_{05} values were obtained and will be used to estimate risks to listed monocot and dicot plant species. Although soil formation of NC 8493 may make it available to plants via run-off, because the parent is already toxic to plants (herbicidal) and risk concerns have previously been identified a degradate toxicity study to terrestrial plants is not likely to add significant value to the risk assessment.

Ethofumesate is translocated to foliage following emerging shoot and root absorption, however it is not translocated from treated foliage. While adult honeybees have not displayed much sensitivity to ethofumesate on an acute contact or oral exposure basis, larval studies are not available and will be necessary to proceed with assessing risk to bees. Additionally, if ethofumesate can be translocated to foliage after root uptake it is reasonable to expect it can also be translocated to pollen and nectar. The extent to which this is possible is uncertain and could also be an additional exposure route to pollinators. Studies to determine the sensitivity of other life-stages (larvae) and possibly the extent to which ethofumesate is translocated to other parts of the plant (e.g. residues in pollen and nectar) could be necessary to appropriately assess risk to pollinators.

Table 11.2. Aquatic Ecological Effects Data for Ethofumesate and Remaining Data Gaps

OCSPP Guideline	Data Requirement	Submitted Studies (MRID)	Study Classifications	Are data needed to conduct risk assessment?	Justification and Assumptions EPA will Make in Absence of Data
850.1010	Freshwater invertebrate acute toxicity	115063	Supplemental	**Yes**	**A new acute toxicity study is requested for freshwater invertebrates**. The existing study is based on nominal concentrations with no additional measurements of the test substance concentration, or analysis on the purity of the test substance. Additionally, dilution water was obtained from the field and the recommended maximum solvent concentration was exceeded.
		41970702	Invalid		
		00048754	Invalid		
850.1025 850.1035	Saltwater invertebrate acute toxicity	42388101 (mollusk)	Acceptable	No	--
		42364502 (mysid)	Acceptable		

OCSPP Guideline	Data Requirement	Submitted Studies (MRID)	Study Classifications	Are data needed to conduct risk assessment?	Justification and Assumptions EPA will Make in Absence of Data
850.1075	Freshwater fish acute toxicity (rainbow trout)	46546301 (TGAI[1])	Acceptable	No	--
		40098001 (TGAI, TEP[2])	Supplemental		
	Freshwater fish acute toxicity (bluegill sunfish)	42015501 (TGAI)	Acceptable		
		40098001 (TGAI, TEP)	Supplemental		
850.1075	Saltwater fish acute toxicity (Sheepshead minnow)	42409301	Acceptable	No	--
850.1300	Freshwater invertebrate life cycle	42871901	Acceptable	No	--
		41554103	Supplemental		
850.1350	Saltwater invertebrates life cycle	(None)	N/A	**Yes**	**The mysid (and oyster) were both more sensitive on an acute basis than the freshwater daphnid. Consequently a definitive chronic estuarine/marine endpoint would greatly reduce uncertainty in the risk assessment**. In the absence of chronic life-cycle for an estuarine/marine invertebrate an Acute to Chronic ratio (ACR) will be used to estimate a chronic endpoint.
850.1400	Freshwater fish early-life stage	42008901	Acceptable	No	--

OCSPP Guideline	Data Requirement	Submitted Studies (MRID)	Study Classifications	Are data needed to conduct risk assessment?	Justification and Assumptions EPA will Make in Absence of Data
850.1400	Saltwater fish early-life stage	(None)	N/A	No	The RED did not identify chronic risks to freshwater fish, a taxa with comparable sensitivity to estuarine/marine fish (about equal) on an acute exposure basis. **In the absence of data the freshwater fish chronic endpoint will be used as a surrogate to characterize chronic risk to estuarine/marine fish. Alternatively, an acute toxicity test with the fathead minnow would allow EFED to calculate an ACR to estimate a chronic estuarine/marine fish endpoint**.
850.1500	Fish life cycle	(None)	N/A	No	Chronic risks were not identified in the RED based on the freshwater fish ELS endpoint. A full-fish lifecycle is not requested.
850.1735	Whole sediment – Acute Toxicity Invertebrates, Freshwater	(None)	N/A	No	Not required based on chemical properties. See sediment guidance for additional information[3].
Non-guideline	Whole sediment – chronic freshwater invertebrates	(None)	N/A	No	Not required based on chemical properties. See sediment guidance for additional information[3].
850.1740	Whole sediment – Acute Toxicity Invertebrates, Marine	(None)	N/A	No	Not required based on chemical properties. See sediment guidance for additional information[3].
850.4400	Aquatic vascular plant toxicity	46450701	Supplemental	No	The supplemental studies are considered scientifically sound and can be used for risk assessment.
		48958701	Supplemental		
		48566601	Supplemental		

OCSPP Guideline	Data Requirement	Submitted Studies (MRID)	Study Classifications	Are data needed to conduct risk assessment?	Justification and Assumptions EPA will Make in Absence of Data
850.4500	Algal toxicity	41987601 (green algae)	Acceptable	**Yes**	Three species, a freshwater algae, freshwater diatom, and estuarine/marine diatom are required. Only data for green algae are available. **Data to evaluate the relative sensitivities of non-vascular plant species are required for risk assessment (TGAI)[4]. Data are requested for a freshwater diatom, marine diatom, and cyanobacteria.**
850.4550	Cyanobacteria toxicity	(None)	N/A	**Yes**	

[1]TGAI = technical grade active ingredient
[2]TEP = typical end-use product
[3]Sediment guidance available at http://www2.epa.gov/sites/production/files/2015-08/documents/toxtesting_ecoriskassessmentforbenthicinvertebrates.pdf
[4]Normally testing with TEP is preferred, but TGAI is requested for consistency with existing aquatic plant studies.

Table 11.3 Terrestrial Ecological Effects Data for Ethofumesate and Remaining Data Gaps

OCSPP Guideline	Data Requirement	Submitted Studies (MRID)	Study Classifications	Are data needed for risk assessment?	Justification and Assumptions EPA will Make in Absence of Data
850.2100	Avian oral toxicity	115064 (bobwhite)	Acceptable	**Yes**	**Avian acute oral toxicity data for a passerine species are required under the new 40 CFR Part 158. Passerine birds may utilize metabolic pathways that are different from larger birds. In the absence of these data, passerine toxicity data for surrogate pesticides may be used to characterize the toxicity of ethofumesate to passerine species.**
		115065 (mallard)	Acceptable		
850.2200	Avian dietary toxicity	41949202 (bobwhite)	Acceptable	**Yes**	**The major degradate NC 8493is formed up to 30% in soil photolysis studies. A dietary exposure is possible for foraging avian**
		137921 (bobwhite - TEP)	Acceptable		

OCSPP Guideline	Data Requirement	Submitted Studies (MRID)	Study Classifications	Are data needed for risk assessment?	Justification and Assumptions EPA will Make in Absence of Data
		41949201 (mallard)	Acceptable		**species. A dietary study is recommended with the mallard duck or bobwhite quail to confirm potential toxicity of the degradate NC 8493to avian species. Additional studies may be requested based on toxicity results.**
		159176 (mallard)	Acceptable		
850.2300	Avian reproduction	45818111 (bobwhite)	Acceptable	No	--
		45855503 (mallard)	Acceptable		
Non-guideline	Avian inhalation	(None)	N/A	No	--
850.3020	Honeybee adult acute contact toxicity	41970703	Acceptable	No	--
850.3030	Honeybee residue on foliage	(None)	N/A	No	Not required as acute contact toxicity endpoint is >11 µg/bee.
850.3040 (Tier III)	Field testing for pollinators	(None)	N/A	**Yes**	**Additional full field or feeding studies may be necessary if risk concerns are identified for bees at the tier I level. A protocol should be submitted in advance of conducting the study.**
Non-guideline (OECD 213)	Honeybee adult acute oral toxicity	41970703	Acceptable	No	--

OCSPP Guideline	Data Requirement	Submitted Studies (MRID)	Study Classifications	Are data needed for risk assessment?	Justification and Assumptions EPA will Make in Absence of Data
Non-guideline (Tier I)	Honeybee adult chronic toxicity	(None)	N/A	**Yes**	**Exposure is possible through direct contact of food items, or movement of ethofumesate through the plant to tissues utilized by pollinators. A 10-day adult feeding test should be performed with ethofumesate (TGAI[1]). OECD guidance for assessing chronic (10-day) oral toxicity to honeybee adults is currently in development. A protocol should be submitted in advance of conduction the study.**
Non-guideline (Tier I)	Honeybee larval chronic toxicity (including acute endpoints)	(None)	N/A	**Yes**	**Exposure is possible through direct contact of food items, or movement of ethofumesate through the plant to tissues utilized by pollinators. A chronic larval test should be performed with ethofumesate (TGAI). Both an acute and chronic endpoint are needed. The 21-day larval toxicity study currently under development by OECD[6] provides both acute and chronic oral toxicity data on developing bee brood. Alternatively, separate acute (single dose) and chronic (repeat dose) toxicity tests can be performed. A protocol should be submitted in advance of conducting the study**

6 http://www.oecd.org/chemicalsafety/testing/Draft_GD_honeybee_larval_tox_repeated_exposure_25_February_2014.pdf

OCSPP Guideline	Data Requirement	Submitted Studies (MRID)	Study Classifications	Are data needed for risk assessment?	Justification and Assumptions EPA will Make in Absence of Data
Non-guideline (Tier II)	Residues in pollen and nectar	(None)	N/A	**Yes**	**Additional studies may be necessary if risk concerns are identified for bees at the tier I level. A protocol should be submitted in advance of conducting the study**.
Non-guideline (Tier II)	Semi-field testing for pollinators (tunnel or colony feeding studies)	(None)	N/A	**Yes**	**Additional semi-field studies may be necessary if risk concerns are identified for juvenile bees at the tier I level. A protocol should be submitted in advance of conducting the study.**
850.4100	Seedling Emergence and Seedling Growth	48690103	Acceptable	No	--
850.4150	Vegetative Vigor	48690103	Acceptable	No	--

[1]TGAI = technical grade active ingredient
[2]TEP = typical end-use product
[3] The study is currently under review and a final determination has not yet been made.

Additional justification for non-guideline data requests:

Study Title: Tier 1- Adult Honeybee Chronic Oral Toxicity
Rationale for Requiring the Data
Terrestrial invertebrates are likely to be impacted if exposed to pesticides in various use settings. Pesticide residues may be transferred to pollen and/or nectar of treated plants and subsequently brought back to the hive. Therefore, potential chronic effects to adult honeybees and other pollinators from oral exposure to some pesticides could exist. Currently available toxicity studies do not address possible lethal and sublethal effects of chronic oral exposure on adult terrestrial invertebrates and will assist in determining whether the sensitivity of adult bees differs from that of earlier life stages. Because of the potential for pollen and nectar to be contaminated with pesticide residues, and subsequently brought back to the hive, it is important to determine the chronic oral toxicity of this compound to adult honeybees and other pollinators. The Office of Pesticide Programs has made available a guidance regarding ecological testing for invertebrates with the honeybee. The guidance discusses Tier I laboratory-based chronic oral toxicity studies of individual adult honeybees as a critical component of the screening-level risk assessment process for examining potential risks from specific routes of exposure. The guidance can be found at: http://www2.epa.gov/pollinator-protection/pollinator-risk-assessment-guidance. Study design elements for the chronic 10-day oral toxicity test with honeybees are similar to the OECD Test Guideline 213 acute oral toxicity test http://www.oecd-ilibrary.org/environment/test-no-213-honeybees-acute-oral-toxicity-test_9789264070165-en.
Practical Utility of the Data
How will the data be used?

The Tier I chronic oral toxicity data on adult bees serve as a foundation for the screening-level assessment of potential risk to non-target organisms including federally listed threatened or endangered species and non-listed terrestrial invertebrate insects, including pollinators, from chronic oral exposures to pesticides. The data will be used to reduce uncertainties associated with the risk assessment for terrestrial invertebrates and will improve EPA's understanding of the potential direct and indirect lethal and sublethal effects on a broad range of terrestrial species, particularly insect pollinators and to determine whether adult toxicity differs substantially from other life stages evaluated in other Tier I tests. If chronic oral effects data for adults are not available, risks to terrestrial insects from chronic oral exposure will be assumed.

How could the data impact the Agency's future decision-making?
The data will inform the determination required under FIFRA or the ESA as to whether continued registration of a pesticide is likely to result in unreasonable adverse effects to non-target species or is likely to adversely affect listed threatened or endangered species and/or their designated critical habitat. Without these data, EPA may need to presume risk which will limit the flexibility of pesticide products to comply with FIFRA and the ESA, and could result in use restrictions.

Study Title: Tier 1- Larval Honeybee Acute Oral Toxicity

Rationale for Requiring the Data

Terrestrial invertebrates are likely to be impacted if exposed to pesticides in various use settings. With eusocial bees, pesticide residues may be transferred to pollen and/or nectar of treated plants and subsequently brought back to the hive where developing larvae and pupae may be exposed. Therefore, potential adverse effects to developing bees could result from exposure to pesticide residues. Available toxicity studies do not address possible effects on brood (larvae and pupae) survival/development. Because of the potential for pollen and nectar to be contaminated with pesticide residues, and subsequently brought back to the hive, it is important to determine the acute toxicity of this compound to bee brood.

The Office of Pesticide Programs has made available a guidance regarding ecological testing for bees using the honey bee as a surrogate test species. The guidances discusses Tier 1 laboratory-based acute toxicity studies of individual honey bee larvae as a critical component of the screening-level risk assessment process for examining potential risks from specific routes of exposure. The guidance be found at: http://www2.epa.gov/pollinator-protection/pollinator-risk-assessment-guidance. Additional guidance on larval honey bee toxicity test design can be found in OECD Test Guideline 237 (http://www.oecd-ilibrary.org/docserver/download/9713171e.pdf?expires=1422485600&id=id&accname=guest&checksum=D8E07C2B1DF77BF096C3B29F55BF86A7). In some cases, information pertaining to acute toxicity to honey bee larvae may be obtained with the chronic honey bee larval test thereby negating the need for separate acute and chronic larval toxicity tests.

Practical Utility of the Data

How will the data be used?
The Tier 1 acute toxicity data on honey bee larvae serve as a foundation for the screening-level assessment of potential risk to non-target organisms including federally listed threatened or endangered and non-listed terrestrial invertebrates, including pollinators, and/or modify their designated critical habitat from acute exposures to pesticides. The data will be used to reduce uncertainties associated with the risk assessment for terrestrial invertebrates and will improve EPA's understanding of the potential effects on terrestrial species and whether there is a differential sensitivity of larval bees relative to adult bees. If acute effects data for larvae are not available, risks to terrestrial insects from acute exposure will be assumed.
How could the data impact the Agency's future decision-making?
The data will inform the determination required under FIFRA or the ESA as to whether continued registration of a pesticide is likely to result in unreasonable adverse effects to non-target species or is likely to adversely affect listed threatened or endangered species and/or modify their designated critical habitat. Without these data, EPA may need to presume risk which will limit the flexibility of pesticide products to comply with FIFRA and the ESA, and could result in use restrictions.

Study Title: Tier 1- Larval Honeybee Chronic Oral Toxicity
Rationale for Requiring the Data
Terrestrial invertebrates are likely to be impacted if exposed to pesticides in various use settings. For eusocial bees, pesticide residues may be transferred to pollen and/or nectar of treated plants and subsequently brought back to the hive where larvae and pupae may be exposed. Therefore, potential effects to developing bees could result from chronic exposure to pesticide residues. Available toxicity studies do not address possible chronic effects on brood (larvae and pupae) survival. Because of the potential for pollen and nectar to be contaminated with pesticide residues, and subsequently brought back to the hive, it is important to determine chronic larval/pupal toxicity and whether adult emergence is adversely affected. This study will provide information on whether honey bee larvae differ in sensitivity from adult bees following chronic exposure. The Office of Pesticide Programs has made available a guidance regarding ecological testing for bees using the honey bee as a surrogate test species. The guidances discusses Tier 1 laboratory-based chronic toxicity studies of individual honey bee larvae as a critical component of the screening-level risk assessment process for examining potential risks from specific routes of exposure. The guidance can be found at: http://www2.epa.gov/pollinator-protection/pollinator-risk-assessment-guidance. Additional information on larval honey bee toxicity repeat exposure test design can be found in the OECD draft guidance (http://www.oecd.org/env/ehs/testing/Draft_GD_honeybees_rep_exp_for_2nd_CR_25_November_2013.pdf). Although study design elements for the chronic 21-day toxicity test with honey bee larvae have been drafted, EPA requires that the proposed protocol for this study be submitted for review and approval by EPA prior to initiating the test.
Practical Utility of the Data
How will the data be used? The Tier 1 chronic toxicity data on bee larvae serve as a foundation for the screening-level assessment of potential risk to non-target organisms including federally listed threatened or endangered and non-listed terrestrial invertebrates, including insect pollinators, from chronic exposures to pesticides. These data will be used to reduce uncertainties associated with the risk assessment for terrestrial invertebrates and will improve EPA's understanding of the potential direct and indirect lethal and sublethal effects on a broad range of terrestrial species, particularly insect pollinators. These data will also assist in determining whether early life stages of the bee differ in their sensitivity to pesticides relative to adults. If chronic effects data for larvae are not available, risks to terrestrial insects from chronic exposure will be assumed. **How could the data impact the Agency's future decision-making?** The data will inform the determination required under FIFRA or the ESA as to whether continued registration of a pesticide is likely to result in unreasonable adverse effects to non-target species or is likely to adversely affect listed threatened or endangered species and/or modify their designated critical habitat. Without these data, EPA may need to presume risk which will limit the flexibility of pesticide products to comply with FIFRA and the ESA, and could result in use restrictions.

Study Title: Tier II - Semi-Field Testing with Honeybee Colonies
Rationale for Requiring the Data
Bees can be exposed to pesticides through multiple pathways including contact with sprays and dusts and through ingestion of residues in food/water (e.g., pollen/nectar and water used to maintain colony temperature). Worker bees foraging on flowers for pollen and nectar can be exposed to residues in pollen and nectar either through direct contamination of these matrices by foliar sprays and/or dusts. Residues can in turn be brought back to bee colonies where in-hive bees including young adult and developing brood (i.e., eggs, larvae and pupae) may be exposed. EPA guidance on assessing the risk of pesticides to bees identifies a tiered process where the initial screen is based on a suite of acute and chronic laboratory studies individual adult bees and larvae. If screening-level assessment indicates potential chronic risks to individual bees, then higher-tier, semi-field testing studies may be required to examine potential effects at the colony level. Ethofumesate is an insect growth regulator that is applied to a variety of crops that rely on insect pollination. Residues on these crops can provide a route of exposure to foraging pollinators.

Practical Utility of the Data
How will the data be used? If acute tests with larval bees indicate that the ethofumesate is toxic to juvenile bees on an acute contact exposure basis and further effects are observed in chronic tests to individual bees, or acute and chronic test on honeybee larva, tier II studies such as the semi-field tests are needed (and may be requested) to determine whether whole colonies can be affected. If tests indicate that ethofumesate is toxic to juvenile bees on an acute or chronic exposure basis and further effects are observed in chronic tests to individual bees, or acute and chronic test on honeybee larva, tier II studies such as the semi-field tests may be needed to determine whether whole colonies can be affected. Pollen/nectar residue data may be required to refine the risk assessment to bees **How could the data impact the Agency's future decision-making?** Risk estimates based on these data will be considered along with other lines of evidence to determine whether higher-tier studies are needed at the whole-colony level to more precisely characterize the effects of real-world application.

Study Title: Tier II - Residues in Pollen and Nectar
Rationale for Requiring the Data
Terrestrial invertebrates are likely to be impacted if exposed to pesticide residues in various use settings. Pesticide residues may be transferred to pollen and/or nectar of treated plants and subsequently brought back to hive where all life stages may be exposed. For some pesticides, the quantification of pollinator-relevant residues in treated flowering plants is needed, since pollinators will be exposed to residues from either current or prior season applications (due to the potential for residues to accumulate in plants and trees). Residues in edible/transportable-to-hive parts of treated trees and plants, including (where appropriate), but not limited to, guttation water, sap/resins, whole plant tissue (*e.g.*, leaves, stems), as well as blooming, pollen-shedding, and nectar producing parts (*i.e.*, flowers and, if present, extra-floral nectaries) of plants may inform the potential for risk. Studies should be designed to provide residue data for crops and application methods of concern. The Office of Pesticide Programs has made available a guidance regarding ecological testing for invertebrates with the honeybee. The guidance can be found at: http://www2.epa.gov/pollinator-protection/pollinator-risk-assessment-guidance.
Practical Utility of the Data
How will the data be used? Measured residue data will be used to refine conservative estimates of pesticide exposure and reduce uncertainties associated with the Tier I exposure assessment by providing direct measurements of pesticide concentrations resulting from actual use settings. Measured residues may provide a more realistic understanding of exposure through contact or ingestion with which to calculate risk quotients for individual bees as well as to characterize exposure to the colony. If measured residue data are not available, risk estimates for terrestrial insects will be based on model-generated or default values used to support the screening-level assessment. **How could the data impact the Agency's future decision-making?** The data will inform the determination required under FIFRA or the ESA as to whether continued registration of a pesticide is likely to result in unreasonable adverse effects to non-target species or is likely to adversely affect federally listed threatened or endangered species or their designated critical habitat. Without these data, EPA will have to rely on conservative estimates of exposure which will limit the flexibility of pesticide products to comply with FIFRA and the ESA, and could result in use restrictions.

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Appendix 1. Ethofumesate Uses and Application Rates

Use	Maximum Single Application Rate lb ai	Maximum Number of Applications per Year[V] (minimum application interval in days unless specified)	Maximum Yearly Application Rate in lbs of ai	Method of Application
Beets	1.9	2 (NS)	3.0	Soil Band, Soil broadcast.
Sugar Beets	3.75	1[w]	4.0	Band, Broadcast, Soil band, Soil Broadcast
Sugar Beets	1.5	3 (NS)	4.0	Broadcast, Soil treatment
Carrot	1.875	2 (NS)	4.0	Band, Broadcast, Soil band, Soil Broadcast
Garlic, Onion, Shallot	1	3[X] (NS)	3.0	Broadcast, Soil band, Soil Broadcast
Grasses grown for seed	1.875	NS[Y] (NS)	NS	Broadcast, Banded, Spray
Ornamental lawns, turf, sod farms	1.875	3 (NS)	5.6[Z]	Broadcast, Spray

Abbreviations: NS = Not specified

[v] Some labels do not list the max number listed per year OR crop cycle. Number could be assumed based on the maximum yearly rate

[w] Assumed from max application rate and maximum yearly application

[X] Some uses give a lower application rate e.g. 0.4 lb ai/A and list 4 as max per crop cycle but does not get to yearly max. The number 3 is assumed based on the maximum yearly rate (which is in terms of season on the labels)

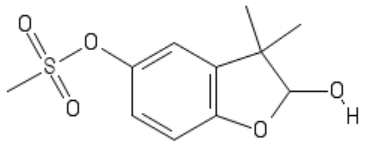
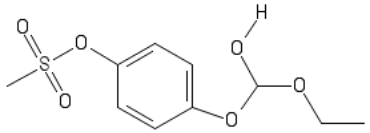
[Y] Some registration say 1 application per crop cycle

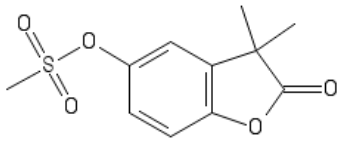
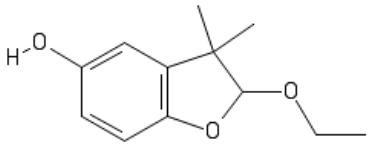
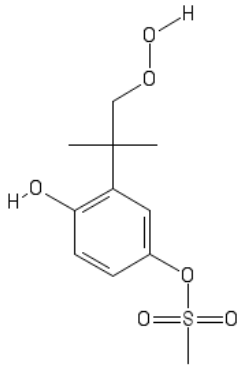
[Z] Assumed from max number of apps at highest application rate

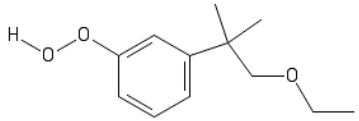
Appendix 2. Previous Actions for Uses of Ethofumesate

Crop	Application Rate (lb ai/A)		Number of applications (Application Interval in Days)	Action/DP Barcode/Date	Comments
	Single	Seasonal/ Annual			
Sugar beets	1.875	NS	NS	Initial Registration 10065-L 5/24/76	Minimal risk to non-target organisms
Ryegrass Kentucky Bluegrass and Bentgrass	1.875 1.125	NS	NS	Section 3 New Uses Reg. No. 40546-5 1/25/80	
Perennial Ryegrass Seed	1.5	N/A	1	Section 18 Emergency Exemption Washington 2/5/78	
Annual Ryegrass (ground)	1.5	N/S	N/S	Section 18 Emergency Exemption Oregon 9/16/77	60,000 lbs ai max on 40,000 acres in 1977
Ryegrass Kentucky Bluegrass Bent grass Fescues	1.875	NS	NS	Section 5 Experimental Use Permit 10065-EUP-5 6/8/76 10065-EUP-8 8/25/76	EUP-5 – extension of permit up to 500 acres treated
Sugar Beets	1.875	NS	NS	Section 5 Experimental Use Permit 10065-EUP-4 5/7/76	
Sugar Beets	3.75	NS	NS	Section 5 Experimental Use Permit 10065-EUP 3/16/76	
Sugar Beets, Swiss Chard, Spinach, Grass Seed, Turf, Sod, Carrots (IR-4), Garden Beets, Bulb Onions	3.75	9.0	NS	Section 4 D269242 RED 6/15/04 8/31/05 (Revised)	Presents the greatest risks to freshwater fish and non-target terrestrial plants through runoff and spray drift

Appendix 3. Structures of Ethofumesate's Degradates

Code Name/ Synonym	Chemical Name/ Smiles Code	Chemical Structure	Study Type/ Corresponding OCSPP Guideline	MRID	Maximum % AR (interval)[1]
Major (>10%) Transformation Products					
NC 8493NC 8493	2,3-dihydro-2-hydroxy-3, 3-dimethyl-5-benzofuranyl methanesulphonate O(C1C(C2=C(O1)C=CC(=C2)O[S](=O)(=O)C)(C)C)[H]		Soil Photolysis 835.2410	41214205	29.8 (Day 9)
			Aerobic Soil Metabolism 835.4200	42413001	5.93 (day 30)
			Anaerobic Soil Metabolism 835.4200	44731914	0.71 (day 151)
Component A	Unidentified CCOC(OC1=CC=C(C=C1)O[S](=O)(=O)C)O[H]		Aquatic Photolysis 835.2240	46157901	17.6 (day 6)
Unidentified	Unidentified	---	Aerobic Aquatic Metabolism 835.4300	42413001	18.4 (day 103)
Unextractable Residue	---	---	Aerobic Soil Metabolism 835.4200	42413001	57.3 (day 365)
			Anaerobic Soil Metabolism 835.4200	44731914	25.3 (day 159)
			Aerobic Aquatic Metabolism 835.4300	42413001	14.2 (day 103)
CO_2	Carbon Dioxide	O=C=O	Aerobic Soil Metabolism 835.4200	42413001	21.9 (day 365)
			Aerobic Aquatic Metabolism 835.4300	42413001	1.5 (day 103)
Minor (<10%) Transformation Products					
NC 9607			Aerobic Soil Metabolism 835.4200	42413001	1.9 (day 30)[1]

Code Name/ Synonym	Chemical Name/ Smiles Code	Chemical Structure	Study Type/ Corresponding OCSPP Guideline	MRID	Maximum % AR (interval)[1]
	2,3-dihydro-3, 3-dimethyl-2-oxobenzofuran-5-yl methanesulfonate C1(C(C2=C(O1)C=CC(=C2)O[S](=O)(=O)C)(C)C)=O		Anaerobic Soil Metabolism 835.4200	44731914	1.2 (day 30)
NC 10458	2-ethoxy-2, 3-dihydro-3, 3-dimethyl-5-hydroxy benzofuran CCOC1C(C2=C(O1)C=CC(=C2)O[H])(C)C		Aquatic Photolysis 835.2240	46157901	5.2 (day 5)
NC 20645	2-(2-hydroxy-5-methanesulfoxy-phenyl)-2-methylpropanoic acid C(C1=C(C=CC(=C1)OS(=O)(=O)C)O[H])(C)(C)CO O[H]		Aerobic Soil Metabolism 835.4200	44731912 44731913	0.57 (30 days)

Code Name/ Synonym	Chemical Name/ Smiles Code	Chemical Structure	Study Type/ Corresponding OCSPP Guideline	MRID	Maximum % AR (interval)[1]
Component B	CCOCC(C1=CC=CC(=C1)OO[H])(C)C		Aquatic Photolysis 835.2240	46157901	4.9 (day 3 day)
[1]Observed at a moisture content of 1.75%W/W.					

Appendix 4. Available Ecotoxicity studies for Ethofumesate

Table A4.1. Available Terrestrial Toxicity Studies for Ethofumesate

Taxonomic Group	Study Type	Surrogate Species	Toxicity Value	Acute Toxicity Classification	Source and Classification
Birds	Acute oral	Bobwhite quail (*Colinus virginianus*)	LD_{50} > 8743 mg ai/kg-bw No effects	Practically non-toxic	115064 Acceptable
	Acute oral	Mallard duck (*Anas platyrhynchos)*	LD_{50} > 3445 mg ai/kg-bw No effects	Practically non-toxic	115065 Supplemental
	Acute dietary	Bobwhite quail (*Colinus virginianus*)	LC_{50} > 5200 mg ai/kg-diet NOAEC ≥ 5200 mg ai/kg-diet No effects	Practically non-toxic	41949201 Acceptable
			LC_{50} > 5200 mg ai/kg-diet NOAEC ≥ Not reported No effects	Practically non-toxic	ACC127694 Acceptable
	Acute dietary	Mallard duck (*Anas platyrhynchos)*	LC_{50} > 5200 mg ai/kg-diet NOAEC ≥ 5200 mg ai/kg-diet No effects	Practically non-toxic	41949202 Acceptable
			LC_{50} > 10000 mg ai/kg-diet NOAEC ≥ Not reported No effects	Practically non-toxic	ACC225319 Acceptable
	Chronic reproduction	Bobwhite quail (*Colinus virginianus*)	NOAEC ≥ 3240 mg ai/kg-diet LOAEC > 3240 mg ai/kg-diet No effects reported	--	45818111 Acceptable
	Chronic reproduction	Mallard duck (*Anas platyrhynchos)*	NOAEC ≥ 3069 mg ai/kg-diet LOAEC > 3069 mg ai/kg-diet No effects reported	--	45855503 Acceptable

Taxonomic Group	Study Type	Surrogate Species	Toxicity Value	Acute Toxicity Classification	Source and Classification
Mammals	Acute oral	Laboratory rat (Rattus norvegicus)	LD_{50} > 6400 mg ai/kg-bw No effects	Practically non-toxic	41214215 Acceptable
			LD_{50} > 6400 mg ai/kg-bw No effects	Practically non-toxic	242165 Acceptable
		Rabbit (TEP 42%)	LD_{50} > 6400 mg ai/kg-bw No effects	Practically non-toxic	238000 Acceptable
		Laboratory rat (TEP 20%) (Rattus norvegicus)	LD_{50} = 5660 mg ai/kg-bw Sublethal effects: Dyspnea, weakness, collapse	Practically non-toxic	No MRID recoded Supplemental
		Guinea pig	LD_{50} > 1200 mg ai/kg-bw No effects reported	Practically non-toxic	2397 Acceptable
	Sub-chronic Dietary	Mouse	NOAEC ≥ 1250 mg ai/kg-diet LOAEC > 1250 mg ai/kg-diet No effects	--	ACC23800 Acceptable (non-guideline)
		Dog	NOAEC ≥ 4000 mg ai/kg-diet LOAEC > 20000 mg ai/kg-diet Increased SOPT, SAP, Liver weights in females	--	ACC23800 Acceptable (non-guideline)

Taxonomic Group	Study Type	Surrogate Species	Toxicity Value	Acute Toxicity Classification	Source and Classification
	Developmental toxicity	Laboratory rat (Rattus norvegicus	NOAEC ≥ 100 mg ai/kg-diet LOAEC > 1000 mg ai/kg-diet Post dose salivation and reduced food consumption	--	ACC243885 Acceptable (non-guideline)
	Chronic Reproduction	Laboratory rat (Rattus norvegicus)	NOAEC ≥ 5000 mg ai/kg-diet LOAEC > 5000 mg ai/kg-diet No effects	--	92063034 Acceptable
Terrestrial insects	Acute contact	Honeybee (*Apis mellifera*)	LD_{50} > 50 µg ai/bee NOAEC ≥ 50 µg ai/bee No effects	Practically non-toxic	45638220 Acceptable
	Acute oral	Honeybee (*Apis mellifera*)	LD_{50} > 50 µg ai/bee NOAEC ≥ 50 µg ai/bee No effects	Practically non-toxic	41970703 Acceptable

Taxonomic Group	Study Type	Surrogate Species	Toxicity Value	Acute Toxicity Classification	Source and Classification
Terrestrial plants	Vegetative vigor	Monocot Onion (*Allium cepa*), corn (*Zea mays*), oat (*Avena sativa*), wheat (*Triticum aestivum*) Dicot carrot (*Daucus carota*, cucumber (*Cucumis sativus*), soybean (*Glycine max*), lettuce (*Lactuca sativa*), tomato (*Lycopersicum esculentum*), radish (*Raphanus sativus*)	Monocot (wheat) EC_{25} = 0.24 lb ai/A NOAEC = 0.16 lb ai/A Based on dry weight Dicot (Soybean)* EC_{25} = 0.09 lb ai/A EC_{05} = 0.003 lb ai/A NOAEC < 0.16 lb ai/A Based on height Dicot (Radish)* EC_{25} = 0.21 lb ai/A EC_{05} = 0.000024 lb ai/A NOAEC < 0.16 lb ai/A Based on dry weight Phytotoxic effects in all species included chlorosis, necrosis, leaf dormancy, stem desiccation.	--	45874701 Acceptable
	Seedling emergence	Monocot Onion (*Allium cepa*), corn (*Zea mays*), oat (*Avena sativa*), wheat (*Triticum aestivum*) Dicot carrot (*Daucus carota*, cucumber (*Cucumis sativus*), soybean (*Glycine max*), lettuce (*Lactuca sativa*), tomato (*Lycopersicum esculentum*), radish (*Raphanus sativus*)	Monocot (wheat) EC_{25} = 0.15 lb ai/A NOAEC = 0.08 lb ai/A Based on dry weight Dicot (lettuce) EC_{25} = 0.18 lb ai/A NOAEC = 0.16 lb ai/A Based on dry weight Phytotoxic effects in all species included chlorosis, necrosis, leaf dormancy, stem desiccation.	--	45814702 Acceptable

*Both dicots will be used to characterize risks based on radish having the less sensitive EC25 but more sensitive EC05 than soybean (more sensitive EC25 but less sensitive EC05)

Table A4.2. Available Aquatic Toxicity Studies for Ethofumesate

Taxonomic Group	**Study Type**	**Surrogate Species**	**Toxicity Value**	**Acute Toxicity Classification**	**Source and Classification**
Freshwater Fish	Acute	Rainbow trout (*Oncorhynchus mykiss*)	LC_{50} = 11.52 mg ai/L NOAEC (visually estimated) = 3.73 mg ai/L LOAEC = 7.31 mg ai/L LOAEC based on sublethal effects: darkened appearance, loss of equilibrium, lethargy and loss of balance	Slightly toxic	46578951 Acceptable
			LC_{50} = 180 mg ai/L NOAEC (estimated) = 56.73 mg ai/L	Slightly toxic	ACC232242 Acceptable
			LC_{50} = 30mg ai/L NOAEC not reported	Slightly toxic	No MRID Supplemental
			LC_{50} = 0.75 mg ai/L NOAEC not reported	Very highly toxic	40098001 Supplemental
			LC_{50} = 0.5 mg ai/L NOAEC not reported (TEP – 25%)	Very highly toxic	40098001 Supplemental
			LC_{50} = 13 mg ai/L NOAEC not reported	Slightly toxic	No MRID Supplemental
		Bluegill sunfish	LC_{50} = 21.8 mg	Slightly toxic	42015501

Taxonomic Group	**Study Type**	**Surrogate Species**	**Toxicity Value**	**Acute Toxicity Classification**	**Source and Classification**
		(*Lepomis macrochirus*)	ai/L NOAEC (visually estimated) = 15.6 mg ai/L Based on sublethal effects: darkened appearance, loss of equilibrium, lethargy and loss of balance		Acceptable
			LC_{50} > 320 mg ai/L NOAEC (estimated) = 56. mg ai/L	Practically Non-toxic	ACC232242 Acceptable
			LC_{50} = 17.5 mg ai/L NOAEC not reported (TEP – 20%)	Very highly toxic	No MRID Supplemental
			LC_{50} = 2.5 mg ai/L NOAEC not reported	Moderately toxic	40098001 Supplemental
			LC_{50} = 6.5 mg ai/L NOAEC not reported (TEP – 25%)	Moderately toxic	40098001 Supplemental
		Feeder fish (*Poecilia reticulata*)	LC_{50} = 15 mg ai/L NOAEC not reported (TEP – 19%)	Slightly toxic	No MRID Supplemental
	Chronic (Early Life-	Fathead minnow	NOAEC = 2.56	--	42008901

Taxonomic Group	**Study Type**	**Surrogate Species**	**Toxicity Value**	**Acute Toxicity Classification**	**Source and Classification**
	Stage)	(*Pimephales promelas*)	mg ai/L LOAEC = 4.17 mg ai/L Based on length and wet weight		Acceptable
Estuarine/marine fish	Acute	Sheepshead minnow (*Cyprinodon variegatus*)	LC_{50} = 25.0 mg ai/L NOAEC = 12.0 mg ai/L LOAEC = 19.0 mg ai/L LOAEC based on sublethal effects: lethargy and loss of equilibrium	Slightly Toxic	42409301 Acceptable
Freshwater invertebrates	Acute	Waterflea (*Daphnia magna*)	EC_{50} = 294 mg ai/L Sublethal effects not reported	Practically non-toxic	115063 Supplemental
			EC_{50} = 64 mg ai/L NOAEC Not Recoded	Practically non-toxic	ACC231232 Supplemental
	Chronic	Waterflea (*Daphnia magna*)	NOAEC = 0.3 mg ai/L LOAEC = 0.6 mg ai/L Based on offspring production)	--	42871901 Acceptable
			NOAEC = 0.25 mg ai/L LOAEC = 0.75 mg ai/L Based on offspring production)	--	41554103 Supplemental
Estuarine/marine invertebrates	Acute	Eastern oyster (*Crassostrea virginica*)	EC_{50} = 2.6 mg ai/L NOAEC (estimated) = 0.8 mg ai/L	Moderately toxic	42388101 Acceptable

Taxonomic Group	**Study Type**	**Surrogate Species**	**Toxicity Value**	**Acute Toxicity Classification**	**Source and Classification**
			LOAEC (estimated) = 2.0 mg ai/L Based on shell deposition		
	Acute	Mysid shrimp (*Americamysis bahia*)	LC_{50} = 5.3 mg ai/L NOAEC < 2.5 mg ai/L LOAEC = 2.5 mg ai/: LOAEC estimated based sublethal effects: Surfacing, lethargy, erratic swimming	Moderately toxic	42364502 Acceptable
Aquatic plants	Non-vascular (TGAI)	Green algae (*Raphidocelis subcapitata*)	<u>Cell Density, Growth Rate, and Biomass</u> EC_{50} > 2.76 mg ai/L NOAEC > 2.76 mg ai/L LOAEC > 2.76 mg ai/L No effects	--	41687601 Acceptable
	Vascular (TGAI)	Duckweed (*Lemna minor*)	<u>Number of fronds</u> EC_{50} = 39.0 mg ai/L NOAEC = 0.76 mg ai/L LOAEC = 1.9 mg ai/L <u>Growth</u> EC_{50} > 52.8 mg ai/L NOAEC = 4.3 mg ai/L LOAEC = 10.0 mg ai/L <u>Biomass</u>	--	46450701 Supplemental

Taxonomic Group	**Study Type**	**Surrogate Species**	**Toxicity Value**	**Acute Toxicity Classification**	**Source and Classification**
			EC_{50} > 52.8 mg ai/L NOAEC = 0.76 mg ai/L LOAEC = 1.9 mg ai/L		

Appendix 5. Screening Level Models to Evaluate Potential Importance of Drinking Water and Inhalation Exposure Pathways

SIP (Screening Imbibition Program, v1.0) was used to calculate an upper bound estimate of ethofumesate exposure via drinking water using solubility (53.7 mg/L), the most sensitive acute and chronic avian toxicity endpoints (bobwhite quail, LD_{50} > 3445 mg ai/kg-bw; bobwhite quail and mallard duck NOAEC > 3240 and > 3069 mg ai/kg-diet respectively) and the most sensitive acute and chronic mammalian toxicity endpoints (rat LD_{50} >6400 mg ai/kg-bw and NOAEL > 5000 mg ai/kg-bw). The model indicated that there are no acute or chronic concerns to birds and mammals through the drinking water exposure pathway (Tables A4.1 and A4.2).

Table A4.1. SIP Mammalian Results for Ethofumesate

Parameter	**Acute**	**Chronic**
Upper bound exposure (mg/kg-bw)	9.2364	9.2364
Adjusted toxicity value (mg/kg-bw)	4922.6276	3845.8028
Ratio of exposure to toxicity	0.0019	0.0024
Conclusion*	**Drinking water exposure alone is NOT a potential concern for mammals**	**Drinking water exposure alone is NOT a potential concern for mammals**

Table A4.2. SIP Avian Results for Ethofumesate

Parameter	**Acute**	**Chronic**
Upper bound exposure (mg/kg-bw)	43.4970	43.4970
Adjusted toxicity value (mg/kg-bw)	1788.7315	152.2610
Ratio of exposure to acute toxicity	0.0243	0.2857
Conclusion*	**Drinking water exposure alone is NOT a potential concern for birds**	**Drinking water exposure alone is NOT a potential concern for birds**

*Conclusion is for drinking water exposure alone. This does not combine all routes of exposure. Therefore, when aggregated with other routes (*i.e.*, diet, inhalation, dermal), pesticide exposure through drinking water may contribute to a total exposure that has potential for effects to non-target animals.

STIR (Screening Tool for Inhalation Risk, v1.0) was used to calculate an upper bound estimate of ethofumesate exposure via inhalation using molecular weight (286.3 g/mole), vapor pressure (2.17×10^{-7} mm Hg), high end application rate (Ground: 3.75 lb ai/A), most sensitive acute avian toxicity endpoint (bobwhite quail, LD_{50} > 3445 mg ai/kg-bw), and most sensitive acute oral and inhalation mammalian toxicity endpoints (rat, LD_{50} >6400 mg ai/kg-bw and 4-hr LC_{50} > 2.05 mg ai/L, respectively). There is an acceptable study with a lower non-definitive NOAEL for inhalation in rats (>0.49 mg ai/L). Comparing, this non-definitive endpoint does present a potential inhalation risk concern for birds. However, the > 2.05 mg ai/L endpoint does not indicate an avian inhalation risk concern. Since both values are greater than, for comparison the 2.05 mg ai/L endpoint was used. The results also indicated that inhalation alone is not likely a potential pathway of concern for mammals (Tables A4.3 and A4.4).

Table A4.3. STIR Avian (0.020 kg) Results for Ethofumesate

Maximum Vapor Concentration in Air at Saturation (mg/m^3)	3.34E-03	
Maximum 1-hour Vapor Inhalation Dose (mg/kg)	4.20E-04	
Adjusted Inhalation LD_{50}	4.47E+00	
Ratio of Vapor Dose to Adjusted Inhalation LD_{50}	9.40E-05	**Exposure not Likely Significant**
Maximum Post-treatment Spray Inhalation Dose (mg/kg)	3.96E-01	
Ratio of Droplet Inhalation Dose to Adjusted Inhalation LD_{50}	8.87E-02	**Exposure not Likely Significant**

Table A4.4. STIR Mammalian (0.15 kg) Results for Ethofumesate

Maximum Vapor Concentration in Air at Saturation (mg/m^3)	3.34E-03	
Maximum 1-hour Vapor Inhalation Dose (mg/kg)	5.28E-04	
Adjusted Inhalation LD_{50}	1.22E+02	
Ratio of Vapor Dose to Adjusted Inhalation LD_{50}	4.33E-06	**Exposure not Likely Significant**
Maximum Post-treatment Spray Inhalation Dose (mg/kg)	4.98E-01	
Ratio of Droplet Inhalation Dose to Adjusted Inhalation LD_{50}	4.08E-03	**Exposure not Likely Significant**